

Application No. 09/675,525  
Amendment dated February 24, 2005  
Amendment under 37 CFR 1.116 Expedited Procedure Examining Group

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently amended) A ~~replicable-genetic package~~ bacteriophage displaying a compound other than a polypeptide expressed by the ~~replicable-genetic package~~ bacteriophage, wherein the ~~replicable-genetic package~~ bacteriophage comprises a heterologous nucleic acid tag that can be decoded to identify a characteristic of the compound, and the heterologous nucleic acid tag is a nucleic acid segment other than a segment that encodes for a polypeptide displayed on the replicable-genetic package bacteriophage.

2-3. (cancel)

4. (Withdrawn and currently amended) The ~~replicable-genetic package~~ bacteriophage of claim [[3]] 1, wherein the bacteriophage is a filamentous phage.

5. (Currently amended) The ~~replicable-genetic package~~ bacteriophage of claim [[3]] 1, wherein the bacteriophage is a non-filamentous phage.

6. (Currently amended) The ~~replicable-genetic package~~ bacteriophage of claim [[3]] 1, wherein the bacteriophage is an icosahedral phage.

7. (Currently amended) The ~~replicable-genetic package~~ bacteriophage of claim 1, wherein the compound is a small molecule.

8. (Currently amended) The ~~replicable-genetic package~~ bacteriophage of claim 1, wherein the compound comprises a polypeptide linked to a small molecule.

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9. (Currently amended) The ~~replicable-genetic-package bacteriophage~~ of claim 1, wherein if the compound is a peptide then the ~~replicable-genetic-package bacteriophage~~ and the compound are attached by other than a peptide linkage.

10. (Withdrawn and currently amended) The ~~replicable-genetic-package bacteriophage~~ of claim 1, wherein the ~~replicable-genetic-package bacteriophage~~ and compound are joined via a covalent bond formed between an endogenous functional group on the ~~bacteriophage-replicable-genetic-package~~ and a functional group borne by the compound.

11. (Currently amended) The ~~replicable-genetic-package bacteriophage~~ of claim 1, wherein the ~~replicable-genetic-package bacteriophage~~ bears a package linker and the compound is attached to the ~~replicable-genetic-package bacteriophage~~ by association with the package linker.

12. (Currently amended) The ~~replicable-genetic-package bacteriophage~~ of claim 1, wherein the compound bears a compound linker and the compound is attached to the ~~replicable-genetic-package bacteriophage~~ via the compound linker.

13. (Withdrawn and currently amended) The ~~replicable-genetic-package bacteriophage~~ of claim 1, wherein the ~~replicable-genetic-package bacteriophage~~ bears a package linker and the compound a compound linker and the compound is attached to the ~~replicable-genetic-package bacteriophage~~ by association of the linkers.

14. (Withdrawn and currently amended) The ~~replicable-genetic-package bacteriophage~~ of claim 13, wherein the ~~replicable-genetic-package bacteriophage~~ and the compound are linked by a non-covalent interaction.

15. (Withdrawn and currently amended) The ~~replicable-genetic-package bacteriophage~~ of claim 13, wherein the package linker and compound linker are members of a binding pair.

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16. (Withdrawn and currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 15, wherein binding pair members comprise a binding protein and a ligand having specific binding affinity for the binding protein.

17. (Withdrawn and currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 16, wherein the binding protein is an antibody and the ligand is a hapten.

18. (Withdrawn and currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 15, wherein the binding pair members comprise biotin and either avidin, streptavidin or neutravidin.

19. (Withdrawn and currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 15, wherein the binding pair members comprise peptide dimerization domains.

20. (Withdrawn and currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 13, further comprising a bridging linker that effects association of the package linker and the compound linker.

21. (Withdrawn and currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 20, wherein at least one of the linkers is a reversible linker.

22. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 1, wherein the ~~replicable-genetic-package~~ bacteriophage displays a plurality of compounds.

23. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 22, wherein the ~~replicable-genetic-package~~ is a phage and the plurality of compounds are attached to different coat proteins having different sequences, and each of the different coat proteins bears one or more of the compounds.

24. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 23, wherein the plurality of compounds are the same.

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25. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 24, wherein at least some of the plurality of compounds are different.

26. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 22, wherein ~~the replicable-genetic-package is a phage and~~ the plurality of compounds are attached to a plurality of coat proteins having the same sequence, and each of the plurality of coat proteins bears one or more of the compounds.

27. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 26, wherein the plurality of compounds are the same.

28. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 26, wherein at least some of the plurality of compounds are different.

29. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 22, wherein the plurality of compounds are attached to a single coat protein.

30. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 22, wherein ~~the replicable-genetic-package is a phage and~~ bacteriophage bears a plurality of exogenous attachment sites of the same type on a single coat protein or a plurality of coat proteins of the same sequence such that each of the coat proteins bear one or more of the attachment sites, and the plurality of compounds are associated with the ~~replicable-genetic-package~~ bacteriophage via the attachment sites.

31. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 22, wherein the ~~replicable-genetic-package~~ bacteriophage is a phage and bears a plurality of exogenous attachment sites of the same type on a plurality of coat proteins having different sequences such that each of the coat proteins bear one or more of the attachment sites, and the plurality of compounds are associated with the ~~replicable-genetic-package~~ bacteriophage via the attachment sites.

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32. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 22, wherein the ~~replicable-genetic-package is a phage and~~ bacteriophage bears a plurality of exogenous attachment sites of different types on a single coat protein or a plurality of coat proteins of the same sequence such that each of the coat proteins bear one or more of the attachment sites, and the plurality of compounds are associated with the bacteriophage ~~replicable-genetic-package~~ via the attachment sites.

33. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 22, wherein the ~~replicable-genetic-package is a phage and~~ the bacteriophage bears a plurality of exogenous attachment sites of different types on a plurality of coat proteins having different sequences such that each of the coat proteins bear one or more of the attachment sites, and the plurality of compounds are associated with the ~~replicable-genetic-package~~ bacteriophage via the attachment sites.

34. (Canceled)

35. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 1, wherein the heterologous nucleic acid tag encodes the identity of the compound.

36. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 1, wherein the heterologous nucleic acid tag encodes a value or symbol assigned to the compound.

37. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 1, wherein

(a) ~~the bacteriophage is a phage; and~~

(b) the heterologous nucleic acid tag is inserted into a segment of the genome of the ~~phage~~ bacteriophage such that it is flanked by a heterologous promoter and a heterologous restriction site, the heterologous promoter being in operable linkage with the heterologous nucleic acid tag.

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38. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim 37, wherein the heterologous promoter is selected from the group consisting of a phage T7 promoter, a T3 promoter and a sp6 promoter.

39. (Canceled)

40. (Currently amended) The ~~replicable-genetic-package~~ collection of bacteriophage of claim ~~127~~ 39, wherein each of the heterologous nucleic acid tags from the different ~~replicable-genetic-package~~ bacteriophage are isothermal tags.

41. (Cancel)

42. (Currently amended) The ~~replicable-genetic-package~~ collection of bacteriophage of claim ~~39~~ 127, wherein each ~~replicable-genetic-package~~ bacteriophage bears a different compound from a combinatorial library of small molecules.

43. (Withdrawn and currently amended) The ~~collection of replicable-genetic package~~ bacteriophage of claim ~~39~~ 127, wherein at least a plurality of the ~~replicable-genetic packages~~ bacteriophages are directly attached to the compound by a covalent bond formed from an endogenous functional group on the ~~replicable-genetic-package~~ bacteriophage and a functional group borne by the compound.

44. (Currently amended) The ~~replicable-genetic-package~~ collection of bacteriophage of claim ~~39~~ 127, wherein at least a plurality of the ~~replicable-genetic-package~~ bacteriophage s are attached to the compound via one or more linkers.

45. (Currently amended) A ~~replicable-genetic-package~~ bacteriophage displaying a compound other than an expressed polypeptide, wherein the ~~replicable-genetic package~~ bacteriophage and the compound are attached via a linker.

46. (Currently amended) The ~~replicable-genetic-package~~ bacteriophage of claim ~~45~~ 1, wherein the ~~replicable-genetic-package~~ bacteriophage is a collection of ~~replicable~~

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~~genetic packages~~ bacteriophages, each ~~replicable genetic package~~ bacteriophage in the collection bearing a different compound.

47. (Currently amended) The ~~replicable genetic package~~ bacteriophage of claim 45, wherein the compound is a small molecule.

48. (Cancel)

49. (Currently amended) The ~~replicable genetic package~~ bacteriophage of claim 45, wherein the linker is a package linker attached to the ~~replicable genetic package~~ bacteriophage and the compound is attached to the ~~replicable genetic package~~ bacteriophage via the package linker.

50. (Currently amended) The ~~replicable genetic package~~ bacteriophage of claim 45, wherein the linker is a compound linker borne by the compound and the ~~replicable genetic package~~ bacteriophage is attached to the compound via the compound linker.

51. (Withdrawn and currently amended) The ~~replicable genetic package~~ bacteriophage of claim 45, wherein the linker is a package linker borne by the ~~replicable genetic package~~ bacteriophage, and the compound bears a compound linker and the compound is attached to the ~~replicable genetic package~~ bacteriophage by association of the package and compound linkers.

52. (Withdrawn and currently amended) The ~~replicable genetic package~~ bacteriophage of claim 51, wherein the ~~replicable genetic package~~ bacteriophage and the compound are attached via a non-covalent interaction between package and compound linkers.

53. (Withdrawn and currently amended) The ~~replicable genetic package~~ bacteriophage of claim 51, wherein the ~~replicable genetic package~~ bacteriophage and the compound are attached via a covalent bond formed between package and compound linkers.

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54. (Currently amended) The ~~replicable genetic package bacteriophage~~ of claim 45, wherein the ~~replicable genetic package bacteriophage~~ displays a plurality of compounds.

55.-106 (Canceled)

107. (Withdrawn and currently amended) A method of screening a library of compounds, comprising:

(a) providing a plurality of different ~~replicable genetic packages bacteriophages~~, each ~~as defined by claim 1 displaying a compound other than an expressed polypeptide~~, different ~~replicable genetic packages bacteriophages~~ displaying different compounds and harboring different heterologous nucleic acid tags;

(b) assaying the plurality of ~~replicable genetic packages bacteriophages~~ to identify at least one ~~replicable genetic package bacteriophage~~ displaying at least one compound with a desired property; and

(c) decoding the heterologous nucleic acid tag of the at least one ~~replicable genetic package bacteriophage~~ to identify a characteristic of the at least one compound with the desirable property.

108. (Withdrawn and currently amended) The method of claim 107, wherein the nucleic acid tag is a nucleic acid segment other than a segment that encodes for an expressed polypeptide displayed by the ~~replicable genetic package bacteriophage~~.

109. (Withdrawn and currently amended) The method of claim 107, further comprising for each compound to be screened, contacting the compound with a ~~replicable genetic package bacteriophage~~, different compounds being contacted with different ~~replicable genetic packages bacteriophages~~, thereby forming the plurality of different ~~replicable genetic packages bacteriophages~~.



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110. (Withdrawn and currently amended) The method of claim 109, further comprising generating a correspondence regime indicating which compound is attached to which ~~replicable genetic package~~ bacteriophage.

111. (Withdrawn and currently amended) The method of claim 110, wherein the correspondence regime is a correspondence regime between compounds and the heterologous nucleic acid tags harbored by the ~~replicable genetic packages~~ bacteriophages, and the characteristic of the at least one compound is determined by matching the sequence of the heterologous nucleic acid tag of the at least one ~~replicable genetic package~~ bacteriophage and a sequence of a heterologous nucleic acid tag in the correspondence regime.

112. (Withdrawn and currently amended) The method of claim 109, wherein each compound is contacted with one or more ~~replicable genetic packages~~ bacteriophages that each harbor the same heterologous nucleic acid tag, whereby each ~~replicable genetic package~~ bacteriophage bears a single type of compound and ~~replicable genetic packages~~ bacteriophages harboring the same heterologous nucleic acid tags display the same compound and ~~replicable genetic packages~~ bacteriophages harboring different heterologous nucleic acid tags display different compounds.

113. (Withdrawn and currently amended) The method of claim 109, wherein  
(a) the compounds to be screened are combined into a plurality of pools and each pool is contacted with one or more ~~replicable genetic packages~~ bacteriophages that harbor the same heterologous nucleic acid tag, whereby each of the plurality of ~~replicable genetic packages~~ bacteriophages display a plurality of different compounds; and

(b) assaying comprises  
(i) assaying the plurality ~~replicable genetic packages~~ bacteriophages to identify an initial ~~replicable genetic package~~ bacteriophage displaying a plurality of compounds wherein at least one of the plurality of compounds has the desired activity; and  
(ii) repeating the assay with a set of ~~replicable genetic packages~~ bacteriophages, wherein each member of the set displays one of the compounds borne by the

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initial ~~replicable-genetic-package bacteriophage~~ to identify the at least one ~~replicable-genetic package bacteriophage~~.

114. (Withdrawn and currently amended) The method of claim 107, wherein the decoding step is performed by sequencing the heterologous nucleic acid tag of the at least one ~~replicable-genetic-package bacteriophage~~.

115. (Withdrawn and currently amended) The method of claim 107, wherein the decoding comprises:

- (a) generating a nucleic acid probe from the at least one ~~replicable-genetic package bacteriophage~~, the nucleic acid probe comprising or being complementary to the heterologous nucleic acid tag of the at least one ~~replicable-genetic-package bacteriophage~~; and
- (b) contacting the probe to the heterologous nucleic acid tag from the different ~~replicable-genetic-packages bacteriophages~~ to identify the ~~replicable-genetic-package bacteriophage~~ to which the at least one compound was attached.

116. (Withdrawn and currently amended) The method of claim 115, further comprising determining the identity of the at least one compound from a correspondence regime between different ~~replicable-genetic-packages bacteriophages~~ and different compounds.

117. (Withdrawn and currently amended) The method of claim 115, wherein the ~~replicable-genetic-packages bacteriophages~~ are arranged in an array for the contacting step.

118. (Withdrawn and currently amended) The method of claim 107, wherein the desired property is selected from the group consisting of the capacity to bind to a receptor, the capacity to be transported into or through a cell, the capacity to be a substrate or inhibitor for an enzyme, the capacity to kill bacteria fungi or other microorganisms, and the capacity to agonize or antagonize a receptor.

119. (Withdrawn and currently amended) The method of claim 118, wherein the desired property is capacity to bind a receptor and the assaying step comprises contacting the ~~replicable-genetic-packages bacteriophages~~ displaying different compounds with the receptor

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and identifying at least one ~~replicable-genetic package~~ bacteriophage displaying a compound that binds to the receptor.

120. (Withdrawn and currently amended) The method of claim 118, wherein the desired property is the capacity to be transported into or through a cell and the assaying step comprises contacting the ~~replicable-genetic packages~~ bacteriophages displaying different compounds with the cell and identifying at least one ~~replicable-genetic package~~ bacteriophage displaying a compound that is transported into or through the cell.

121. (Withdrawn and currently amended) The method of claim 118, wherein the desired property is capacity to be a substrate or inhibitor of an enzyme and the assaying step comprises contacting the plurality of ~~replicable-genetic packages~~ bacteriophages with the enzyme and identifying at least one ~~replicable-genetic package~~ bacteriophage displaying a compound that is a substrate or an inhibitor of the enzyme.

122.-126. (Canceled)

127. (Currently Amended) A collection of ~~replicable-genetic packages~~ bacteriophages, each displaying a compound other than a polypeptide expressed by the ~~replicable-genetic package~~ bacteriophage and comprising a heterologous nucleic acid tag that can be decoded to identify a characteristic of the compound, and the heterologous nucleic acid tag is a nucleic acid segment other than a segment that encodes for a polypeptide displayed on the bacteriophage, and wherein at least some of the ~~replicable-genetic packages~~ bacteriophages display different compounds and ~~replicable-genetic packages~~ bacteriophages displaying different compounds harbor different tags.